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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,686	08/03/2006	J. Christopher Anderson	54-000330US	8860

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EXAMINER	
GEBREYESUS, KAGNEW H	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,686	ANDERSON ET AL.	
	Examiner	Art Unit	
	KAGNEW H. GEBREYESUS	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *September 12, 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-13,15-19,21 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-13,15-19,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/6/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response on September 12, 2008 to the Office Action dated May 07, 2008 is acknowledged. Applicants have cancelled claims 4, 5, 14, 20, 23-65 without prejudice. Claims 1, 6, 7 and 8 have been amended. Claims 1-3, 6-13, 15-19, 21 and 22 are present for examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 6-13, 15-19, 21 and 22 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue:

"Applicants note that the same independent claim has been carefully considered and found enabled in granted European patent ... Here, we further clarify the claim to address objections of the U.S. Office. To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V.v. Diamond Automation, Inc.,* 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003). Here, as discussed below, the original written description of the invention is exhaustive and shows the inventors possessed the ability to practice the full scope of the inventions, including any desired specific embodiments…"

Applicant's argument has been fully considered but not found persuasive. The granting of a European patent does not preclude the claims from being treated on the merits.

The translation system in claims 1-3, 6, 8-13, 15-19, 21 and 22 comprise a genus of lysyl-O-tRNA or modified variant thereof and a corresponding genus of lysyl-O-RSs described only by a desired function (i.e. suppress a stop or frame shift selector codon with an efficiency of at least 50% compared to the efficiency of the lysyl-O-RS of I41 and/or S268 (mutants of PhΔAD of SEQ ID NO: 28) in combination with the specific lysyl-OtRNA of SEQ ID NO: 26 (derived from a consensus of archaebacterial tRNA sequences). While the specification teaches random mutations followed by screening to identify the lysyl-ORS of I41 and/or S268 (mutants of PhΔAD of SEQ ID NO: 28) derived from a single archaebacterium species (*Pyrococcus horikoshii*) and lysyl-OtRNA of SEQ ID NO: 26, such a screening method is not a substitute for the actual genus of lysyl-ORS and lysyl-OtRNA encompassed in the claimed translation system. The description of a few ORS molecules (the ORS of SEQ ID NO: 28, the I41 and/or the S268 mutants of SEQ ID NO: 28) derived from *Pyrococcus horikoshii* ***[without]*** a description of a common structural attribute that characterizes the claimed genus, is insufficient to describe what broadly encompasses any lysyl-ORS (class I or class II from any source) and corresponding lysyl-OtRNA derived from any biological source.

The specification teaches ORS molecules of SEQ ID NO: 28 (PhΔAD) derived from *Pyrococcus horikoshii* which is a class I lysyl tRNA synthetase. Furthermore the specification teaches how to make the ORS of I41 and S268 which are derivatives of SEQ ID NO: 28 with reduced toxicity. However while the specification teaches these few

class I lysyl tRNA synthetase variants (ORS) from *Pyrococcus horikoshii* it does not disclose a sufficient number of possible ORS variants including class I and class II lysyl tRNA synthetase variants to be in possession of such variants from all possible sources including those from known and yet to be discovered sources.

The specification only teaches generation of a few lysyl-orthogonal synthetases and lysyl-orthogonal tRNA (derived from homologous archaeal lysyl-tRNA sequences) that selectively incorporates the amino acid homoglutamine (hGln) into myoglobin in response to the four-base codon AGGA.

Thus the disclosure of a translation system comprising the lysyl-tRNA with the consensus structure of SEQ ID NO: 26 and *Pyrococcus horikoshii* synthetase mutants, comprising I41 and/or S268 (non-toxic mutants derived from PhΔAD lysyl tRNA synthetase) is insufficient to provide description for a translation system broadly encompassing the entire genus of class I and II lysyl-ORS and the entire genus of O-tRNAs from any source.

Thus one skilled in the art cannot reasonably conclude that the inventor had possession of the entire genus of lysyl tRNA/ORS to be used in the translation system.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, at the time the invention was made, of the specific subject matter claimed. MPEP § 2163 further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not a sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence."

Thus Applicants are not in possession of a translation system comprising any lysyl-O-RS and variants from any source known or yet to be discovered that preferentially charge any lysyl-O-tRNA or any variant from any source with homoglutamine as encompassed in the claims.

Furthermore claim 7 limits the genus of the lysyl-ORS molecules used it does not describe the corresponding O-tRNA structure to be used. Furthermore claim 8 attempts to describe the genus of ORS by a functional limitation with no correlation between the function and structure. Claims 9-12 attempts to narrow the scope of the lysyl-O-tRNA structure used but does not describe the genus of ORS used.

Thus although the claims describe a consensus structure derived from a few of lysyl-O-tRNA molecules (archaebacteria), the claims do not disclose the structure of all possible lysyl-OtRNA and all possible class I and II lysyl-O-RS from any source including humans, plants etc to be used in conjunction with said lysyl-O-tRNA. Therefore, these claims encompass an undefined genus of lysyl-O-tRNA and/or lysyl-O-RS molecules that only fit a desired functional characteristic.

Claims 1-3, 6, 8-11, 15-19, 21 and 22 remain rejected under 35 U.S.C. 112, first paragraph, because while the specification may be enabled for a translation system or a cell co-expressing the specific orthogonal tRNA synthetase of SEQ ID NO: 28 or the I41 or the S268 mutants of SEQ ID NO: 28 that preferentially charges the lysyl-OtRNA of SEQ ID NO: 26 with the unnatural amino acid homoglutamine, it does not provide enablement for a translation system or cell comprising any lysyl-ORS/OtRNA from all possible class I and II lysyl-O-RS from any source including humans, plants, yeast, fungi

etc to be used to suppress a selector codon by preferentially charging a homoglutamine any lysyl-OtRNA with an efficiency of at least 50% compared to the efficiently of the lysyl-O-RS of the lysyl-ORS I41 and/or S268 in combination with the lysyl-O-tRNA of SEQ ID NO: 26.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants argue:

"...*In re Wands,* reversed the PTO's determination that claims directed to methods for detection of hepatitis B surface antigens did not satisfy the enablement requirement. In *Wands,* the court noted that there was no disagreement as to the facts, but merely a disagreement as to the interpretation of the data and the conclusion to be made from the facts.

The Court held that the specification was enabling with respect to the claims at issue and found that "there was considerable direction and guidance" in the specification; there was "a high level of skill in the art at the time the application was filed;" and "all of the methods needed to practice the invention were well known." 858 F.2d at 740, 8 USPQ2d at 1406. After considering all the factors related to the enablement issue, the Court concluded that "it would not require undue experimentation to obtain antibodies needed to practice the claimed invention."/d., 8 USPQ2d at 1407. Here, as in Wands (and discussed above), the level of skill in the art is high and considerable guidance is provided to practice the claimed invention. Further, here the scope of the claims is less broad, the rate experimental of success is higher, and more working examples are provided, than in *Wands.* In the rejections, the Office does not dwell on each *Wands* factor, but lays out a rationale based on 1) variability in the "point of reference" standard translation system for efficiency comparisons, and 2) alleged lack of adequate guidance in teaching the scope of the claimed systems and cells.

Furthermore Applicants argue:

The Action appears to acknowledge at least adequate written description and enablement of compositions comprising mutant RSs derived from *Pyrococcus horikoshii* and O-tRNAs derived from a consensus of archaeal lysyl tRNA, that function to incorporate homoglutamin into a protein. As a preliminary matter, the claims have been amended to further clarify and more precisely define the point of reference standard translation system that was objected to in the Action. Because the standard translation system for comparison focuses on a single, well characterized enabled embodiment (comprising the O-RS of SEQ ID NO: 28, the OtRNA of SEQ ID NO.: 26 and the unnatural amino acid homoglutamine)..."

Applicant's argument has been carefully considered but not found persuasive for the following reasons.

While a method of obtaining a lysyl-O-tRNA and corresponding lysyl ORS derived from a single archaebacterial species that can suppress a selector codon with at least 50% compared to a given pair of ORS/OtRNA may be enabled, the instant claims drawn to translation systems comprising any lysyl-ORS/OtRNA from any source such as from humans, plants, yeast, fungi etc. *per se* thus encompasses an enormous scope of desired products wherein said products fit a desired characteristics (function and efficiency).

In order to enable lysyl-ORS and lysyl-OtRNA within the scope of the instant claims, one of skill in the art would require undue amount of experimentation.

Such experimentation includes, providing any lysyl O-tRNA from any source and a corresponding lysyl-ORS that functions to selectively charge said OtRNA with homoglutamine wherein said ORS is selected from a genus of class I or class II lysyl-ORS from any source (human, plant, yeast, fungi algae etc), deciphering those ORSs that suppress a suppressor codon, determining suppressor efficiency and comparing the efficiency with the efficiency of the lysyl-OtRS of I41 and/or the efficiency of S268 when used with the O-tRNA of SEQ ID NO: 26 and then determining the structure of functional pairs within the scope of the claims i.e. those that have at least 50% suppressor efficiency.

Thus, although Applicants have addressed the issue of a point of reference for a method of comparing suppressor efficiency, they have not addressed the scope of the lysyl ORS and lysyl OtRNA which can be derived from any source because the breadth

of the claims encompasses a translation system or cell co-expressing any lysyl-O-tRNA and any tRNA synthetase and variants thereof from any source with any sequence structure that preferentially charges said lysyl-O-tRNA with homoglutamine. Thus searching for the lysyl-ORS and corresponding lysyl-OtRNA that function in concert within the scope of the claims is enormous. The specification does not provide guidance with regards to the lysyl-tRNA-synthetases and lysyl-tRNA or the modifications required for said lysyl tRNA synthetases and tRNA in view of producing functional complementary orthogonal pairs.

Furthermore while claim 7 limits the scope of the lysyl-ORS molecules used, it does not limit the scope of the corresponding O-tRNA structure to be used. Furthermore claim 8 attempts to limit the scope of ORS by its function it does not limit the scope of the O-RS or the O-tRNA structure encompassed. Claims 9-12 limits the scope of the lysyl-O-tRNA structure used but does not limit the scope of the lysyl-ORS to be used.

In conclusion, Applicants have not taught how to make or use a translation system or cell that co-expresses any lysyl-O-tRNA and/or any lysyl-OtRNA synthetase comprising from any source wherein said lysyl-OtRNA synthetase preferentially charges said lysyl-O-tRNA with a homoglutamine with at least 50% compared to the efficiency of a lysyl O-RS of I41 when used with the lysyl O-tRNA of SEQ ID NO: 26 or the lysyl O-RS of S268 and lysyl ORS of SEQ ID NO 26.

The Examiner finds that one skilled in the art would require additional guidance, such as information regarding the structure of the specific cognate lysyl-tRNA synthetase and a corresponding lysyl-O-tRNA that functions to suppress with the desired efficiency. Without such guidance, the experimentation left to those skilled in the art is undue.

Conclusion

This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee of $510.00.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier. Amendments touching the merits of the application which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

A reply under 37 CFR 1.113 to a final rejection must include the appeal from, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAGNEW H. GEBREYESUS whose telephone number is (571)272-2937. The examiner can normally be reached on 8:30am-5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kagnew H Gebreyesus/
Examiner, Art Unit 1656

/JON P WEBER/
Supervisory Patent Examiner, Art Unit 1656/7